FORM PTO 1390 (REV 5-93) US DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE

TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. §371

ATTORNEY DOCKET NUMBER	U.S. APPLICATION NO. (If known, see 37 CFR 1.5)
2001_0572A	09/831452
	NEW

International Application No.	International Filing Date	Priority Date Claimed
PCT/JP99/06309	November 12, 1999	November 12, 1998

Title of Invention
PROTEIN AMSH AND cDNA THEREOF

Applicant(s) For DO/EO/US
Kazuo SUGAMURA and Nobuyuki TANAKA

Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1. [X] This is a **FIRST** submission of items concerning a filing under 35 U.S.C. §371.

2. [] This is a **SECOND** or **SUBSEQUENT** submission of items concerning a filing under 35 U.S.C. §371.

3. [] This express request to begin national examination procedures (35 U.S.C. §371(f)) at any time rather than delay examination until the expiration of the applicable time limit set in 35 U.S.C. §371(b) and PCT Articles 22 and 39(1).

4. [X] A proper Demand for International Preliminary Examination was made by the 19th month from the earliest claimed priority date.

5. [X] A copy of the International Application as filed (35 U.S.C. §371(c)(2))
   a. [] is transmitted herewith (required only if not transmitted by the International Bureau).
   b. [X] has been transmitted by the International Bureau.
   c. [] is not required, as the application was filed in the United States Receiving Office (RO/US)

6. [X] A translation of the International Application into English (35 U.S.C. §371(c)(2)). **ATTACHMENT A**

7. [] Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. §371(c)(3)).
   a. [] are transmitted herewith (required only if not transmitted by the International Bureau).
   b. [] have been transmitted by the International Bureau.
   c. [] have not been made; however, the time limit for making such amendments has NOT expired.
   d. [] have not been made and will not be made.

8. [] A translation of the amendments to the claims under PCT Article 19.

9. [X] An **unexecuted** oath or declaration of the inventor(s) (35 U.S.C. §371(c)(4)). **ATTACHMENT B**

10. [] A translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. §371(c)(5)).

Items 11. to 14. below concern other document(s) or information included:

11. [X] An Information Disclosure Statement under 37 CFR 1.97 and 1.98. **ATTACHMENT C**

12. [] An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.

13. [X] A FIRST preliminary amendment. **ATTACHMENT D**

    [] A SECOND or SUBSEQUENT preliminary amendment.

14. [] Other items or information:

THE COMMISSIONER IS AUTHORIZED TO CHARGE ANY DEFICIENCY IN THE FEE FOR THIS PAPER TO DEPOSIT ACCOUNT NO. 23-0975.

U.S. APPLICATION NO. (if known) NEW 09/831452	INTERNATIONAL APPLICATION NO. PCT/JP99/06309	ATTORNEY'S DOCKET NO. 2001_0572A

15. [X] The following fees are submitted	CALCULATIONS	PTO USE ONLY
BASIC NATIONAL FEE (37 CFR 1.492(a)(1)-(5)):		
Neither international preliminary examination fee nor international search fee paid to USPTO and International Search Report not prepared by the EPO or JPO $1000.00		
International Search Report has been prepared by the EPO or JPO ..... $ 860.00		
International preliminary examination fee not paid ot USPTO but international search paid to USPTO ..... $ 710.00		
International preliminary examination fee paid to USPTO but claims did not satisfy provisions of PCT Article 33(1)-(4) ..... $ 690.00		
International preliminary examination fee paid ot USPTO and all claims satisfied provisions of PCT Article 33(1)-(4) ..... $ 100.00		
ENTER APPROPRIATE BASIC FEE AMOUNT =	$860.00	
Surcharge of $130.00 for furnishing the oath or declaration later than [] 20 [] 30 months from the earliest claimed priority date (37 CFR 1.492(e)).	$	

Claims	Number Filed	Number Extra	Rate		
Total Claims	-20 =		X $18.00	$	
Independent Claims	- 3 =		X $80.00	$	
Multiple dependent claim(s) (if applicable)			+ $270.00	$	
TOTAL OF ABOVE CALCULATIONS =				$860.00	
[] Small Entity Status is hereby asserted. Above fees are reduced by 1/2.				$	
SUBTOTAL =				$860.00	
Processing fee of $130.00 for furnishing the English translation later than [] 20 [] 30 months from the earliest claimed priority date (37 CFR 1.492(f)). +				$	
TOTAL NATIONAL FEE =				$860.00	
Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). $40 per property +				$	
TOTAL FEES ENCLOSED =				$860.00	
				Amount to be refunded	$
				Amount to be charged	$

a. [X] A check in the amount of $860.00 to cover the above fees is enclosed. A duplicate copy of this form is enclosed.

b. [] Please charge my Deposit Account No. 23-0975 in the amount of $_____ to cover the above fees. A duplicate copy of this sheet is enclosed.

c. [] The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 23-0975.

NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b)) must be filed and granted to restore the application to pending status.

19. CORRESPONDENCE ADDRESS

000513
PATENT TRADEMARK OFFICE

By: Warren M. Cheek Jr.
Warren M. Cheek, Jr.,
Registration No. 33,367

WENDEROTH, LIND & PONACK, L.L.P.
2033 "K" Street, N.W., Suite 800
Washington, D.C. 20006-1021
Phone:(202) 721-8200
Fax:(202) 721-8250

May 10, 2001

[CHECK NO. WWW3]

[2001_0572A]

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of	:	**Confirmation No. 4276**
Kazuo SUGAMURA et al.	:	Docket No. 2001-0572A
Serial No. 09/831,452	:	Group Art Unit Not Yet Assigned
Filed July 10, 2001	:	Examiner Not Yet Assigned
PROTEIN AMSH AND cDNA THEREOF	:	

PRELIMINARY AMENDMENT

Assistant Commissioner for Patents,
Washington, D.C. 20231

Sir:

Responsive to the Notice dated April 29, 2002, please amend the above-identified application as follows:

In the Sequence Listing:

Please replace the Sequence Listing of record with the attached substitute Sequence Listing.

REMARKS

The foregoing amendments are presented to place the application in compliance with the sequence rules under 37 CFR 1.821-1.825.

Applicants have submitted a Sequence Listing in both paper and computer readable form as required by 37 C.F.R. 1.821(c) and (e). Amendments directing its entry into the specification

have also been incorporated herein. The content of the paper and computer readable copies are the same and no new matter has been added.

In view of the foregoing, it is believed that each requirement set forth in the Notice has been satisfied, and that the application is now in compliance with the sequence rules under 37 CFR 1.821-1.825. Accordingly, favorable examination on the merits is respectfully requested.

Respectfully submitted,

Kazuo SUGAMURA et al.

By: _____
Lee Cheng
Registration No. 40,949
Attorney for Applicants

LC/gtn
Washington, D.C. 20006-1021
Telephone (202) 721-8200
Facsimile (202) 721-8250
May 29, 2002

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of	:	**Confirmation No. 4276**
Kazuo SUGAMURA et al.	:	Docket No. 2001-0572A
Serial No. 09/831,452	:	Group Art Unit Not Yet Assigned
Filed July 10, 2001	:	Examiner Not Yet Assigned
PROTEIN AMSH AND cDNA THEREOF	:	

RESPONSE

Assistant Commissioner for Patents,
Washington, D.C. 20231

Sir:

Responsive to the Notice dated April 29, 2002, there is submitted herewith, in a separate Preliminary Amendment, a paper copy of a revised Sequence Listing for the above-identified application which has been prepared in accordance with the sequence rules under 37 CFR 1.821-1.825. The Sequence Listing contains the identical sequences appearing in the original application papers. Thus, no new matter has been added.

There is also submitted herewith a copy of the revised Sequence Listing in computer readable form as required by 37 CFR 1.821(e). The content of the paper and computer readable copies are the same.

A copy of the Notice is also attached as required.

In view of the foregoing, it is believed that each requirement set forth in the Notice has been satisfied, and that the application is now in compliance with the sequence rules under 37 CFR 1.821-1.825. Accordingly, favorable examination on the merits is respectfully requested.

Respectfully submitted,

Kazuo SUGAMURA et al.

By: _____
Lee Cheng
Registration No. 40,949
Attorney for Applicants

LC/gtn
Washington, D.C. 20006-1021
Telephone (202) 721-8200
Facsimile (202) 721-8250
May 29, 2002

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of	:	
Kazuo SUGAMURA et al.	:	**Attn: BOX PCT**
Serial No. NEW	:	**Docket No. 2001_0572A**
Filed May 10, 2001	:	

PROTEIN AMSH AND cDNA THEREOF
[Corresponding to PCT/JP99/06309
Filed November 12, 1999]

PRELIMINARY AMENDMENT

Assistant Commissioner for Patents,
Washington, DC 20231

Sir:

Prior to calculating the filing fee, please amend the above-identified application as follows:

IN THE SPECIFICATION

Page 1, immediately after the title, please insert:

This application is a 371 of PCT/JP99/06309 filed November 12, 1999.

IN THE CLAIMS

Please amend the claims as follows:

5. (Amended) A recombinant vector containing the hAMSH cDNA of claim 3.

11. (Amended) A recombinant vector containing the mAMSH cDNA of claim 9.

Please add the following new claims:

13. A recombinant vector containing the DNA fragment of claim 4.

14. A recombinant vector containing the DNA fragment of claim 10.

REMARKS

The specification has been amended to reflect the 371 status. In addition, the multiple dependencies of the claims have been removed to reduce the PTO filing fee.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached pages are captioned **"Version with markings to show changes made"**.

Favorable action on the merits is solicited.

Respectfully submitted,

Kazuo SUGAMURA et al.

By _____
Warren M. Cheek, Jr.
Registration No. 33,367
Attorney for Applicants

WMC/dlk
Washington, D.C. 20006-1021
Telephone (202) 721-8200
Facsimile (202) 721-8250
May 10, 2001

SEQUENCE LISTING

<110> SUGAMURA, Kazuo
TANAKA, Nobuyuki

<120> Protein AMSH and cDNA thereof

<130> 2001-0572A/LC/00653

<140> 09/831,452
<141> 2001-07-10

<150> PCT/JP99/06309
<151> 1999-11-12

<150> JP No. 10-322674
<151> 1998-11-12

<160> 4

<170> PatentIn Ver. 2.0

<210> 1
<211> 424
<212> PRT
<213> Homo sapiens

<400> 1

```
Met Ser Asp His Gly Asp Val Ser Leu Pro Pro Glu Asp Arg Val Arg
  1               5                  10                  15
Ala Leu Ser Gln Leu Gly Ser Ala Val Glu Val Asn Glu Asp Ile Pro
            20                  25                  30
Pro Arg Arg Tyr Phe Arg Ser Gly Val Glu Ile Ile Arg Met Ala Ser
        35                  40                  45
Ile Tyr Ser Glu Glu Gly Asn Ile Glu His Ala Phe Ile Leu Tyr Asn
    50                  55                  60
Lys Tyr Ile Thr Leu Phe Ile Glu Lys Leu Pro Lys His Arg Asp Tyr
65                  70                  75                  80
Lys Ser Ala Val Ile Pro Glu Lys Lys Asp Thr Val Lys Lys Leu Lys
                85                  90                  95
Glu Ile Ala Phe Pro Lys Ala Glu Glu Leu Lys Ala Glu Leu Leu Lys
            100                 105                 110
Arg Tyr Thr Lys Glu Tyr Thr Glu Tyr Asn Glu Glu Lys Lys Lys Glu
        115                 120                 125
Ala Glu Glu Leu Ala Arg Asn Met Ala Ile Gln Gln Glu Leu Glu Lys
    130                 135                 140
Glu Lys Gln Arg Val Ala Gln Gln Lys Gln Gln Gln Leu Glu Gln Glu
145                 150                 155                 160
Gln Phe His Ala Phe Glu Glu Met Ile Arg Asn Gln Glu Leu Glu Lys
                165                 170                 175
Glu Arg Leu Lys Ile Val Gln Glu Phe Gly Lys Val Asp Pro Gly Leu
            180                 185                 190
Gly Gly Pro Leu Val Pro Asp Leu Glu Lys Pro Ser Leu Asp Val Phe
        195                 200                 205
Pro Thr Leu Thr Val Ser Ser Ile Gln Pro Ser Asp Cys His Thr Thr
    210                 215                 220
Val Arg Pro Ala Lys Pro Pro Val Val Asp Arg Ser Leu Lys Pro Gly
```

```
225                 230                 235                 240
Ala Leu Ser Asn Ser Glu Ser Ile Pro Thr Ile Asp Gly Leu Arg His
                245                 250                 255
Val Val Val Pro Gly Arg Leu Cys Pro Gln Phe Leu Gln Leu Ala Ser
            260                 265                 270
Ala Asn Thr Ala Arg Gly Val Glu Thr Cys Gly Ile Leu Cys Gly Lys
        275                 280                 285
Leu Met Arg Asn Glu Phe Thr Ile Thr His Val Leu Ile Pro Lys Gln
    290                 295                 300
Ser Ala Gly Ser Asp Tyr Cys Asn Thr Glu Asn Glu Glu Glu Leu Phe
305                 310                 315                 320
Leu Ile Gln Asp Gln Gln Gly Leu Ile Thr Leu Gly Trp Ile His Thr
                325                 330                 335
His Pro Thr Gln Thr Ala Phe Leu Ser Ser Val Asp Leu His Thr His
            340                 345                 350
Cys Ser Tyr Gln Met Met Leu Pro Glu Ser Val Ala Ile Val Cys Ser
        355                 360                 365
Pro Lys Phe Gln Glu Thr Gly Phe Phe Lys Leu Thr Asp His Gly Leu
    370                 375                 380
Glu Glu Ile Ser Ser Cys Arg Gln Lys Gly Phe His Pro His Ser Lys
385                 390                 395                 400
Asp Pro Pro Leu Phe Cys Ser Cys Ser His Val Thr Val Val Asp Arg
                405                 410                 415
Ala Val Thr Ile Thr Asp Leu Arg
            420
```

<210> 2
<211> 1910
<212> DNA
<213> Homo sapiens

<221> CDS
<222> 11..1282

<400> 2

```
cttggtcctg atgtctgacc atggagatgt gagcctcccg cccgaagacc gggtgagggc 60
tctctcccag ctgggtagtg cggtagaggt gaatgaagac attccacccc gtcggtactt 120
ccgctctgga gttgagatta tccgaatggc atccatttac tctgaggaag gcaacattga 180
acatgccttc atcctctata acaagtatat cacgctcttt attgagaaac taccaaaaca 240
tcgagattac aaatctgctg tcattcctga aaagaaagac acagtaaaga aattaaagga 300
gattgcattt cccaaagcag aagagctgaa ggcagagctg ttaaaacgat atacccaaga 360
atatacagaa tataatgaag aaaagaagaa ggaagcagag gaattggccc ggaacatggc 420
catccagcaa gagctggaaa aggaaaaaca gagggtagca caacagaagc agcagcaatt 480
ggaacaggaa cagttccatg ccttcgagga gatgatccgg aaccaggagc tagaaaaaga 540
gcgactgaaa attgtacagg agtttgggaa ggtagaccct ggcctaggtg gcccgctagt 600
gcctgacttg gagaagccct ccttagatgt gttccccacc ttaacagtct catccataca 660
gccttcagac tgtcacacaa ctgtaaggcc agctaagcca cctgtggtgg acaggtcctt 720
gaaacctgga gcactgagca actcagaaag tattcccaca atcgatggat tgcgccatgt 780
ggtggtgcct gggcggctgt gcccacagtt tctccagtta gccagtgcca acactgcccg 840
gggagtggag acatgtggaa ttctctgtgg aaaactgatg aggaatgaat ttaccattac 900
ccatgttctc atccccaagc aaagtgctgg gtctgattac tgcaacacag agaacgaaga 960
agaacttttc ctcatacagg atcagcaggg cctcatcaca ctgggctgga ttcatactca 1020
ccccacacag accgcgtttc tctccagtgt cgacctacac actcactgct cttaccagat 1080
gatgttgcca gagtcagtag ccattgtttg ctcccccaag ttccaggaaa ctggattctt 1140
taaactaact gaccatggac tagaggagat ttcttcctgt cgccagaaag gatttcatcc 1200
acacagcaag gatccacctc tgttctgtag ctgcagccac gtgactgttg tggacagagc 1260
agtgaccatc acagaccttc gatgagcgtt tgagtccaac accttccaag aacaacaaaa 1320
```

```
ccatatcagt gtactgtagc cccttaattt aagctttcta gaaagctttg gaagtttttg 1380
tagatagtag aaaggggggc atcacctgag aaagagctga ttttgtattt caggtttgaa 1440
aagaaataac tgaacatatt ttttaggcaa gtcagaaaga gaacatggtc acccaaaagc 1500
aactgtaact cagaaattaa gttactcaga aattaagtag ctcagaaatt aagaaagaat 1560
ggtataatga acccccatat acccttcctt ctggattcac caattgttaa catttttttc 1620
ctctcagcta tccttctaat ttctctctaa tttcaatttg tttatattta cctctgggct 1680
caataagggc atctgtgcag aaatttggaa gccatttaga aaatcttttg gattttcctg 1740
tggtttatgg caatatgaat ggagcttatt actgggggtga gggacagctt actccatttg 1800
accagattgt ttggctaaca catcccgaag aatgattttg tcaggaatta ttgttattta 1860
ataaatattt caggatattt ttcctctaca ataaagtaac aattaactta            1910
```

<210> 3
<211> 424
<212> PRT
<213> mouse

<400> 3

```
Met Ser Asp His Gly Asp Val Ser Leu Pro Pro Gln Asp Arg Val Arg
  1               5                  10                  15
Ile Leu Ser Gln Leu Gly Ser Ala Val Glu Leu Asn Glu Asp Ile Pro
            20                  25                  30
Pro Arg Arg Tyr Tyr Arg Ser Gly Val Glu Ile Ile Arg Met Ala Ser
        35                  40                  45
Val Tyr Ser Glu Glu Gly Asn Ile Glu His Ala Phe Ile Leu Tyr Asn
    50                  55                  60
Lys Tyr Ile Thr Leu Phe Ile Glu Lys Leu Pro Lys His Arg Asp Tyr
65                  70                  75                  80
Lys Ser Ala Ile Ile Pro Glu Lys Lys Asp Ala Val Lys Lys Leu Lys
                85                  90                  95
Ser Val Ala Phe Pro Lys Ala Glu Glu Leu Lys Thr Glu Leu Leu Arg
            100                 105                 110
Arg Tyr Thr Lys Glu Tyr Glu Gln Tyr Lys Glu Arg Lys Lys Lys Glu
        115                 120                 125
Glu Glu Glu Leu Ala Arg Asn Ile Ala Ile Gln Gln Glu Leu Glu Lys
    130                 135                 140
Glu Lys Gln Arg Val Ala Gln Gln Lys Gln Lys Gln Leu Glu Gln Glu
145                 150                 155                 160
Gln Phe His Ala Phe Glu Glu Met Ile Gln Arg Gln Glu Leu Glu Lys
                165                 170                 175
Glu Arg Leu Lys Ile Val Gln Glu Phe Gly Lys Val Asp Pro Gly Pro
            180                 185                 190
Cys Gly Pro Leu Leu Pro Asp Leu Glu Lys Pro Cys Val Asp Val Ala
        195                 200                 205
Pro Ser Ser Pro Phe Ser Pro Thr Gln Thr Pro Asp Cys Asn Thr Gly
    210                 215                 220
Met Arg Pro Ala Lys Pro Pro Val Val Asp Arg Ser Leu Lys Pro Gly
225                 230                 235                 240
Ala Leu Ser Val Ile Glu Asn Val Pro Thr Ile Glu Gly Leu Arg His
                245                 250                 255
Ile Val Val Pro Arg Asn Leu Cys Ser Glu Phe Leu Gln Leu Ala Ser
            260                 265                 270
Ala Asn Thr Ala Lys Gly Ile Glu Thr Cys Gly Val Leu Cys Gly Lys
        275                 280                 285
Leu Met Arg Asn Glu Phe Thr Ile Thr His Val Leu Ile Pro Arg Gln
    290                 295                 300
Asn Gly Gly Pro Asp Tyr Cys His Thr Glu Asn Glu Glu Glu Ile Phe
305                 310                 315                 320
```

```
Phe Met Gln Asp Asp Leu Gly Leu Leu Thr Leu Gly Trp Ile His Thr
                325                 330                 335
His Pro Thr Gln Thr Ala Phe Leu Ser Ser Val Asp Leu His Thr His
            340                 345                 350
Cys Ser Tyr Gln Met Met Leu Pro Glu Ser Ile Ala Ile Val Cys Ser
        355                 360                 365
Pro Lys Phe Gln Glu Thr Gly Phe Phe Lys Leu Thr Asp Tyr Gly Leu
    370                 375                 380
Gln Glu Ile Ser Thr Cys Arg Gln Lys Gly Phe His Pro His Gly Arg
385                 390                 395                 400
Asp Pro Pro Leu Phe Cys Asp Cys Ser His Val Thr Val Lys Asp Arg
                405                 410                 415
Ile Val Thr Ile Thr Asp Leu Arg
            420
```

<210> 4
<211> 1384
<212> DNA
<213> homosapiens

<221> CDS
<222> 56..1327

<400> 4

```
gtgacgtttc cggaagctct gactgtcatc cttcacgaaa gaacttattt gtccaatgtc 60
tgaccatggg gatgtgagcc tcccacccca agaccgggtg aggattctgt cccaacttgg 120
gagtgcagtt gagttaaatg aagacattcc accccgtcgc tactaccgct ccggtgttga 180
gatcatccgc atggcgtccg tttactcgga agaaggcaac attgaacatg cctttatcct 240
ctacaacaag tacatcacgc tgtttattga aaaacttccg aaacaccgag actacaaatc 300
agctatcatt cctgagaaga aagatgctgt caagaaatta aagagcgtcg ctttccctaa 360
agcggaagag ctgaagacag agctcttgag aagatacacc aaagaatatg agcagtataa 420
agagcgaaag aaaaaggaag aagaggaact tgcccgaaat atcgccatcc agcaagagtt 480
ggaaaaagaa aaacagaggg ttgctcagca gaagcagaag cagctagagc aggagcaatt 540
ccatgccttt gaggagatga tccagaggca ggagctggaa aaagaacggc tgaaaattgt 600
tcaagagttc gggaaggtag accctggccc ctgcgggcct ctgctccctg atctggaaaa 660
gccttgtgta gatgtggccc ccagctcacc gttctcgccc acgcagactc cagactgtaa 720
cacaggcatg aggccagcta agccacctgt ggtggacagg tccctgaaac ctggagcgtt 780
aagcgtcata gaaaatgttc ccaccattga aggcctgcgc cacatcgtgg tgccccgtaa 840
tctgtgctca gaatttctcc agcttgccag tgccaatacc gccaaaggca ttgaaacctg 900
tggagtcctc tgtggaaaac tgatgagaaa tgaattcaca atcacacatg ttctcatccc 960
cagacaaaat ggtgggcctg attattgcca cacggagaat gaagaagaaa ttttctttat 1020
gcaggatgac cttggactcc tcactcttgg ctggatccat actcatccaa cccaaacggc 1080
ctttctgtcc agtgtggatc tccacactca ctgctcctac caaatgatgt taccagagtc 1140
catcgcaatc gtctgttccc caaagttcca ggaaactgga ttctttaagc taactgacta 1200
tggtcttcaa gagatttcaa cctgccggca gaaaggcttt caccccatg gcagagaccc 1260
accgctgttc tgtgactgca gccatgtcac tgtcaaggac agaattgtga cgatcacaga 1320
ccttcgataa atctcaaatc atgaaccagg gagatggatc actgggtaac agcacttgtc 1380
acca                                                          1384
```

DESCRIPTION

Protein AMSH and cDNA thereof

This application is a 371 of PCT/JP99/06309 filed November 12, 1999.

Technical Field

The present invention relates to human protein hAMSH and mouse protein mAMSH, and cDNAs encoding these proteins. More particularly, the present invention relates to novel human and mouse signal transduction molecules, AMSH, human and mouse genes encoding these proteins, cDNAs thereof, and antibodies against these proteins.

Background Art

A variety of cells having different functions should collaborate with each other for expression of higher biological functions such as hematopoietic, immunological and nervous systems. Communication among the cells is essential for their collaborations. Cytokines are known to be the proteins responsible for intercellular communication, and include interleukin (IL)-1 to 18, colony stimulation factors (CSFs), interferons (IFNs) and several chemokines.

Signals are generated by binding of the cytokines to specific receptors on the cell membrane, and survival, proliferation, differentiation and functional expression of the cells are controlled by signal transduction. Accordingly, dysfunction of cytokine-receptor signal transduction pathways result in collapse of the immunological and hematopoietic systems to cause severe infectious diseases, cancers and autoimmune diseases.

CLAIMS

1. A human protein hAMSH having the amino acid sequence of SEQ ID No. 1.

2. A human gene encoding the human protein hAMSH of claim 1.

3. cDNA of the human gene of claim 2, which is hAMSH cDNA having the nucleotide sequence of SEQ ID no. 2.

4. A DNA fragment comprising a partial sequence in the nucleotide sequence of SEQ ID No. 2.

5. A recombinant vector containing the hAMSH cDNA of claim ~~4 or the DNA fragment of claim 4.~~ 3.

6. An antibody against the human protein hAMSH of claim 1.

7. A mouse protein mAMSH having the amino acid sequence of SEQ ID No. 3.

8. A mouse gene encoding the mouse protein mAMSH of claim 7.

9. cDNA of the mouse gene of claim 7, which is mAMSH cDNA having the nucleotide sequence of SEQ ID no. 4.

10. A DNA fragment comprising a partial sequence in the nucleotide sequence of SEQ ID No. 4.

11. A recombinant vector containing the mAMSH cDNA of claim 9~~, or the DNA fragment of claim 10.~~

DESCRIPTION

Protein AMSH and cDNA thereof

Technical Field

The present invention relates to human protein hAMSH and mouse protein mAMSH, and cDNAs encoding these proteins. More particularly, the present invention relates to novel human and mouse signal transduction molecules, AMSH, human and mouse genes encoding these proteins, cDNAs thereof, and antibodies against these proteins.

Background Art

A variety of cells having different functions should collaborate with each other for expression of higher biological functions such as hematopoietic, immunological and nervous systems. Communication among the cells is essential for their collaborations. Cytokines are known to be the proteins responsible for intercellular communication, and include interleukin (IL)-1 to 18, colony stimulation factors (CSFs), interferons (IFNs) and several chemokines.

Signals are generated by binding of the cytokines to specific receptors on the cell membrane, and survival, proliferation, differentiation and functional expression of the cells are controlled by signal transduction. Accordingly, dysfunction of cytokine-receptor signal transduction pathways result in collapse of the immunological and hematopoietic systems to cause severe infectious diseases, cancers and autoimmune diseases.

For the reasons described above, it is quite important to elucidate the intracellular signal transduction pathways mediated by the cytokine/cytokine receptor system. This is important, in order to appreciate the basic phenomena such as proliferation and differentiation of the cells, pathogenesis, diagnosis and therapeutic intervention of various diseases at the molecular levels.

The inventors of the present invention have isolated the genes of "common γ-chain" commonly included in a plurality of the cytokine receptors, and have made a great contribution in elucidating the structure and function of the cytokine receptors. Of particular elucidation is that the γ-chain is an essential subunit for functional expression of IL-2, IL-4, IL-7 and IL-9, and abnormality in the γ-chain causes impairment of early development of T-cells via dysfunction of IL-7 (Science, 262:1874-1877, 1993; Int. Immunol., 6:1451-1454, 1994; Science, 263:1453-1454, 1994; Eur. J. Immunol., 25:3001-3005, 1995).

Recently, the inventors of the present invention have identified "STAMs" as novel signal molecules concerning signal transduction in the proliferating cells by the cytokines, and found that these STAMs are present downstream of the IL-2/GM-CSF receptor and directly associate with JAK3/2. The inventors also found that STAMs play an important role in expression of c-myc and signal transduction for DNA synthesis (Immunity, 6:449-457, 1997).

While several important mechanisms of the intracellular signal transduction pathway by binding of the cytokines to the receptors have been made clear, additional novel molecules should be identified for elucidating the overall structure and function of the intracellular signal transduction pathway, because plural molecules are thought to be continuously and synergetically involved in the signal transduction pathway and to manifest final functional

expression by constructing a so-called cascade.

The present invention was performed by taking the above situations into consideration, and the object of this invention is to provide a novel signal transduction molecules interacting with SH3 domain of a signal molecule STAM that has been found by the present inventors, and exerting essential functions on signal transduction to the downstream from STAM.

Another object of the present invention is to provide gene encoding this novel molecule, cDNA thereof, and antibody against the novel molecule.

Disclosure of Invention

The present invention for solving the foregoing problems provides a human protein hAMSH having the amino acid sequence of SEQ ID No. 1

The present invention also provides a human gene encoding the human protein hAMSH, hAMSH cDNA having the nucleotide sequence of SEQ ID No. 2, and a DNA fragment comprising a partial sequence of SEQ ID No. 2.

The present invention further provides a recombinant vector containing the cDNA or the partial fragment thereof, and an antibody against the human protein hAMSH.

The present invention additionally provides a mouse protein mAMSH having the amino acid sequence of SEQ ID No. 3, a mouse gene encoding the mouse protein mAMSH, mAMSH cDNA having the nucleotide sequence of SEQ ID No. 4, a DNA fragment comprising a partial sequence of SEQ ID No. 4, a recombinant vector containing the cDNA or the DNA fragment thereof, and an antibody against the mouse protein mAMSH.

Best Mode for Carrying Out the Invention

The procedure for obtaining a human protein hAMSH and cDNA thereof, as well as the procedure for identifying the function of the protein will be described hereinafter.

The human protein hAMSH cDNA according to the present invention is a human gene's cDNA isolated by screening a human cDNA library by Far-Western method using a chimera gene of SH3 domain of STAM gene and glutathione-S-transferase (GST). This cDNA has a nucleotide sequence comprising 1910 base pairs shown in SEQ ID No. 2, and encodes the protein hAMSH having the amino acid sequence of SEQ ID No. 1.

While estimated a nucleus transfer signal and a JAB1-like structure are observed in the molecule of the protein hAMSH, this protein is confirmed to be a novel molecule since corresponding molecules are not found in the protein data base.

The facts that this protein hAMSH is a novel molecule involved in signal transduction for cell proliferation by association with STAM, downstream of the cytokine receptor, is confirmed as follows:

(1) AMSH-dc2 in which half of the C-terminal region of hAMSH has been deleted, suppresses signal transduction for DNA synthesis after stimulating with IL-2 and GM-CSF; and

(2) The AMSH-dc2 mutant suppresses c-myc inducing signal transduction after stimulating with IL-2 and GM-CSF.

The cDNA of the mouse protein mAMSH according to the present invention is a mouse gene's cDNA isolated by screening a mouse cDNA

library using the hAMSH cDNA as a probe. This cDNA has the nucleotide sequence comprising 1384 base pairs shown in SEQ ID No. 4, and encodes the protein mAMSH having the amino acid sequence of SEQ ID No. 3.

The proteins hAMSH and mAMSH according to the present invention may be obtained by conventional methods such as isolating from human or mouse organs or from cell lines, preparing the peptides by a chemical synthesis based on the amino acid sequence provided by the present invention, or by a recombinant DNA techniques using the cDNA fragments provided by the present invention. For example, in order to obtain the protein hAMSH by the recombinant DNA technique, RNA is prepared by in vitro transcription from the vectors comprising cDNA fragment having the nucleotide sequence of SEQ ID No. 2, and the protein may be expressed through in vitro translation using the RNA as a template. The protein encoded by the cDNA may be also expressed in large scale in E. coli, Bacillus subtilis, yeast, animal cells and plant cells by recombining an expression vector with the translation region of cDNA by known methods in the art.

When the protein according to the present invention is produced by expression of DNA by in vitro translation, the cDNA or its translation region is recombined into a vector having a RNA polymerase promoter, and the recombinant cDNA is added in an in vitro translation system such as a rabbit dyalyzate or wheat germ extract containing a RNA polymerase for the promoter. Examples of the RNA polymerase promoter include T6, T3 and SP6. Examples of the vector containing these RNA polymerase promoter include pKA1, pCDM8, pT3/7 18, pT7/3 19 and pBlueprint II.

For large scale production of the protein encoded in cDNA in microorganisms such as E. coli, an expression vector is constructed by inserting the cDNA according to the present invention or its translation region into an expression vector comprising an origin suitable for

microorganisms, a promoter, a ribosome binding site, cDNA cloning sites and terminater, followed by cultivation of the transformant cell obtained after translormation of the host cell with the expression vector. A protein containing an arbitrary region can be obtained by allowing the expression vector to express by adding an initiation codon and a stop codon before and after the arbitrary translation region. Otherwise, a desired protein portion can be selectively obtained by allowing the protein to express as a fusion protein with other protein, followed by cleaving this fusion protein with an appropriate protease. Examples of the expression vector for use in E. coli include pUC, pBluescript II, pET expression system and pGEX expression system.

For producing the protein according to the present invention in eukaryotic cell such as animal cells, the cDNA or the translation region thereof is inserted into an expression vector for the eukaryotic cell comprising a promoter, splicing region and poly (A) addition site to introduce the recombinant vector into the eukaryotic cell. Examples of the expression vector include pKA1, pCDM8, pSVK3, pMSG, pSVL, pBK-CMV, pBK-RSV, EBV vector, pRS and pYES2. While cultured cells of a mammal such as monkey kidney cells COS7 and Chinese hamster ovary cells CHO, budding yeast, dividing yeast, silkworm cells and African clawed frog egg cells are usually used as the eukaryotic cells, any eukaryotic cells may be used so long as they are able to express MIST. The expression vector can be introduced into the eukaryotic cell by a conventional method such as an electroporation method, a calcium phosphate method, a liposome method and a DEAE dextran method.

Separation procedures known in the art may be combined for isolating and purifying the desired protein from the culture after expressing the protein in microorganisms or eukaryotic cells. The separation and purifying methods include, for example, treatment with a denaturation reagent such as urea or with a surface active agent, ultrasonic treatment,

enzymatic digestion, salting-out and solvent precipitation method, dialysis, centrifugation, ultrafiltration, gel filtration, SDS-PAGE, isoelectric point electrophoresis, ion exchange chromatography, hydrophobic chromatography, affinity chromatography and reversed phase chromatography.

Peptide fragments (five amino acid residues or more) containing any partial amino acid sequence of the amino acid sequence of SEQ ID Nos 1 and 3 are included in the proteins hAMSH and mAMSH according to the present invention. These peptide fragments may be used for producing antibodies. Fusion proteins with other proteins are also included in the protein according to the present invention.

The gene of the present invention is a human gene encoding the protein described above, and can be isolated, for example, from the existing genome library using the cDNA of the present invention or a partial sequence thereof as a probe.

The cDNA of the present invention may be obtained by screening a cDNA library derived from a human cell or mouse cell through colony or plaque hybridization known in the art by using the oligonucleotide probe synthesized, based on the nucleotide sequence of SEQ ID Nos. 2 and 4. Alternatively, the cDNA of the present invention can be prepared from the mRNA isolated from a human cell or mouse cell by the RT-PCR method using synthesized oligonucleotides that can hybridize to both ends of the cDNA fragment as primers.

Polymorphism due to individual differences is often observed in the animal gene. Accordingly, cDNAs containing an addition or deletion of one or plural nucleotides, and/or substitution with other nucleotides in SEQ ID Nos. 2 and 4 are also included within the scope of the present invention.

Likewise, the proteins containing an addition or deletion of one or

plural amino acids, and/or substitution with other amino acids caused by the alteration of cDNAs may be also included within the scope of the present invention, provided that the protein comprises protein activity pf the protein having the amino acid sequence of SEQ ID No. 1 or 3.

The DNA fragments (10 bp or more) comprising any partial nucleotide sequence of SEQ ID No. 2 or 4 are also included in the DNA fragment of the present invention. DNA fragments comprising sense strand and antisense strand may be categorized into the DNA fragment of the present invention. The DNA fragments can be used as a probe for gene diagnosis.

Antibodies against the proteins of the present invention may be obtained as polyclonal antibodies or monoclonal antibodies by conventional methods using the proteins themselves or partial peptides thereof as antigens.

Example

A part of the hAMSH cDNA (the 383-550th in SEQ ID No. 2: corresponds to the amino acids 125-180th in SEQ ID No. 1) was amplified by PCR and was inserted into the GST fusion protein expression vector. This vector was introduced into E coli for transformation, and this transformant was stimulated with IPTG to induce expression of the GST fusion protein. The induced fusion protein was purified by affinity chromatography using a glutathione column, thereby obtaining the GST fusion protein. An antiserum was obtained by immunizing a rabbit with this GST fusion protein as an antigen.

Industrial Applicability

As hitherto described in detail, the present invention provides novel signal transduction molecules related to the cytokine based signal transduction pathway, and gene engineering materials. These molecules and gene engineering materials are useful for developing diagnostic and therapeutic methods as well as pharmaceuticals for human diseases due to dysfunction of the cytokine based signal transduction pathway such as severe infectious diseases, cancers and autoimmune diseases.

CLAIMS

1. A human protein hAMSH having the amino acid sequence of SEQ ID No. 1.

2. A human gene encoding the human protein hAMSH of claim 1.

3. cDNA of the human gene of claim 2, which is hAMSH cDNA having the nucleotide sequence of SEQ ID no. 2.

4. A DNA fragment comprising a partial sequence in the nucleotide sequence of SEQ ID No. 2.

5. A recombinant vector containing the hAMSH cDNA of claim 4 or the DNA fragment of claim 4.

6. An antibody against the human protein hAMSH of claim 1.

7. A mouse protein mAMSH having the amino acid sequence of SEQ ID No. 3.

8. A mouse gene encoding the mouse protein mAMSH of claim 7.

9. cDNA of the mouse gene of claim 7, which is mAMSH cDNA having the nucleotide sequence of SEQ ID no. 4.

10. A DNA fragment comprising a partial sequence in the nucleotide sequence of SEQ ID No. 4.

11. A recombinant vector containing the mAMSH cDNA of claim 9 or the DNA fragment of claim 10.

12. An antibody against the mouse protein mAMSH of claim 7.

ABSTRACT

This application provides a human protein AMSH having the amino acid sequence of SE ID No. 1 which is a novel signal transduction molecule interacting with the SH3 domain of cytokine based signal transduction molecule STAM; a gene encoding the above AMSH; a cDNA having the nucleotide sequence of SEQ ID No. 2; and antibody against AMSH.

Rev. 3-21-01

Effective March 1998

DECLARATION AND POWER OF ATTORNEY FOR U.S. PATENT APPLICATION

(X) Original () Supplemental () Substitute (X) PCT () DESIGN

As a below named inventor, I hereby declare that: my residence, post office address and citizenship are as stated below next to my name; that I verily believe that I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural inventors are named below) of the subject matter which is claimed and for which a patent is sought on the invention entitled:

Title: PROTEIN AMSH AND cDNA THEREOF

of which is described and claimed in:
() the attached specification, or
(X) the specification in application Serial No. _____, filed May 10, 2001, and with amendments through _____, or
(X) the specification in International Application No. PCT/JP99/06309, filed November 12, 1999, and as amended on _____ (if applicable).

I hereby state that I have reviewed and understand the content of the above-identified specification, including the claims, as amended by any amendment(s) referred to above.

I acknowledge my duty to disclose to the Patent and Trademark Office all information known to me to be material to patentability as defined in Title 37, Code of Federal Regulations, §1.56.

I hereby claim priority benefits under Title 35, United States Code, §119 (and §172 if this application is for a Design) of any application(s) for patent or inventor's certificate listed below and have also identified below any application for patent or inventor's certificate having a filing date before that of the application on which priority is claimed:

COUNTRY	APPLICATION NO.	DATE OF FILING	PRIORITY CLAIMED
Japan	1998-322674	November 12, 1998	Yes

I hereby claim the benefit under Title 35, United States Code §120 of any United States application(s) listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States application in the manner provided by the first paragraph of Title 35, United States Code §112, I acknowledge the duty to disclose information material to patentability as defined in Title 37, Code of Federal Regulations, §1.56 which occurred between the filing date of the prior application and the national or PCT international filing date of this application:

APPLICATION SERIAL NO.	U.S. FILING DATE	STATUS: PATENTED, PENDING, ABANDONED

And I hereby appoint Michael R. Davis, Reg. No. 25,134; Matthew M. Jacob, Reg. No. 25,154; Warren M. Cheek, Jr., Reg. No. 33,367; Nils Pedersen, Reg. No. 33,145; Charles R. Watts, Reg. No. 33,142; and Michael S. Huppert, Reg. No. 40,268, who together constitute the firm of WENDEROTH, LIND & PONACK, L.L.P., as well as any other attorneys and agents associated with Customer No. 000513, to prosecute this application and to transact all business in the U.S. Patent and Trademark Office connected therewith.

I hereby authorize the U.S. attorneys and agents named herein to accept and follow instructions from NISHIZAWA & ASSOCIATES as to any action to be taken in the U.S. Patent and Trademark Office regarding this application without direct communication between the U.S. attorneys and myself. In the event of a change in the persons from whom instructions may be taken, the U.S. attorneys named herein will be so notified by me.

Direct Correspondence to Customer No:	Direct Telephone Calls to:
000513 PATENT TRADEMARK OFFICE	WENDEROTH, LIND & PONACK, L.L.P. 2033 "K" Street, N.W., Suite 800 Washington, D.C. 20006-1021 Phone (202) 721-8200 Fax (202) 721-8250

Full Name of First Inventor	FAMILY NAME SUGAMURA	FIRST GIVEN NAME Kazuo	SECOND GIVEN NAME		
Residence & Citizenship	CITY Miyagi	STATE OR COUNTRY Japan		COUNTRY OF CITIZENSHIP Japan	
Post Office Address	ADDRESS c/o University of Tohoku, Medical Department, 2-1, Seiryo-cho, Aoba-ku, Sendai-shi, Miyagi, Japan	CITY	STATE OR COUNTRY	ZIP CODE	
Full Name of Second Inventor	FAMILY NAME TANAKA	FIRST GIVEN NAME Nobuyuki	SECOND GIVEN NAME		
Residence & Citizenship	CITY Miyagi	STATE OR COUNTRY Japan		COUNTRY OF CITIZENSHIP Japan	
Post Office Address	ADDRESS c/o University of Tohoku, Medical Department, 2-1, Seiryo-cho, Aoba-ku, Sendai-shi, Miyagi, Japan	CITY	STATE OR COUNTRY	ZIP CODE	
Full Name of Third Inventor	FAMILY NAME	FIRST GIVEN NAME	SECOND GIVEN NAME		
Residence & Citizenship	CITY	STATE OR COUNTRY	COUNTRY OF CITIZENSHIP		
Post Office Address	ADDRESS	CITY	STATE OR COUNTRY	ZIP CODE	
Full Name of Fourth Inventor	FAMILY NAME	FIRST GIVEN NAME	SECOND GIVEN NAME		
Residence & Citizenship	CITY	STATE OR COUNTRY	COUNTRY OF CITIZENSHIP		
Post Office Address	ADDRESS	CITY	STATE OR COUNTRY	ZIP CODE	
Full Name of Fifth Inventor	FAMILY NAME	FIRST GIVEN NAME	SECOND GIVEN NAME		
Residence & Citizenship	CITY	STATE OR COUNTRY	COUNTRY OF CITIZENSHIP		
Post Office Address	ADDRESS	CITY	STATE OR COUNTRY	ZIP CODE	

SEQUENCE LISTING

<110> Japan Science and Technology Corporation

<120> Protein AMSH and cDNA thereof

<130> 99-F-054PCT/YS

<140> PCT/JP99/06309

<141> 1999-11-12

<150> JP No. 10-322674

<151> 1998-11-12

<160> 4

<170> PatentIn Ver. 2.0

<210> 1

<211> 424

<212> PRT

<213> Homo sapiens

<400> 1

Met Ser Asp His Gly Asp Val Ser Leu Pro Pro Glu Asp Arg Val Arg
1 5 10 15

Ala Leu Ser Gln Leu Gly Ser Ala Val Glu Val Asn Glu Asp Ile Pro
20 25 30

Pro Arg Arg Tyr Phe Arg Ser Gly Val Glu Ile Ile Arg Met Ala Ser
35 40 45

Ile Tyr Ser Glu Glu Gly Asn Ile Glu His Ala Phe Ile Leu Tyr Asn
50 55 60

Lys Tyr Ile Thr Leu Phe Ile Glu Lys Leu Pro Lys His Arg Asp Tyr
65 70 75 80

Lys Ser Ala Val Ile Pro Glu Lys Lys Asp Thr Val Lys Lys Leu Lys
85 90 95

Glu Ile Ala Phe Pro Lys Ala Glu Glu Leu Lys Ala Glu Leu Leu Lys

100 105 110

Arg Tyr Thr Lys Glu Tyr Thr Glu Tyr Asn Glu Glu Lys Lys Lys Glu

115 120 125

Ala Glu Glu Leu Ala Arg Asn Met Ala Ile Gln Gln Glu Leu Glu Lys

130 135 140

Glu Lys Gln Arg Val Ala Gln Gln Lys Gln Gln Gln Leu Glu Gln Glu

145 150 155 160

Gln Phe His Ala Phe Glu Glu Met Ile Arg Asn Gln Glu Leu Glu Lys

165 170 175

Glu Arg Leu Lys Ile Val Gln Glu Phe Gly Lys Val Asp Pro Gly Leu

180 185 190

Gly Gly Pro Leu Val Pro Asp Leu Glu Lys Pro Ser Leu Asp Val Phe

195 200 205

Pro Thr Leu Thr Val Ser Ser Ile Gln Pro Ser Asp Cys His Thr Thr

210 215 220

Val Arg Pro Ala Lys Pro Pro Val Val Asp Arg Ser Leu Lys Pro Gly

225 230 235 240

Ala Leu Ser Asn Ser Glu Ser Ile Pro Thr Ile Asp Gly Leu Arg His

245 250 255

Val Val Val Pro Gly Arg Leu Cys Pro Gln Phe Leu Gln Leu Ala Ser

260 265 270

Ala Asn Thr Ala Arg Gly Val Glu Thr Cys Gly Ile Leu Cys Gly Lys

275 280 285

Leu Met Arg Asn Glu Phe Thr Ile Thr His Val Leu Ile Pro Lys Gln

290 295 300

Ser Ala Gly Ser Asp Tyr Cys Asn Thr Glu Asn Glu Glu Glu Leu Phe

305 310 315 320

Leu Ile Gln Asp Gln Gln Gly Leu Ile Thr Leu Gly Trp Ile His Thr

325 330 335

His Pro Thr Gln Thr Ala Phe Leu Ser Ser Val Asp Leu His Thr His

340 345 350

Cys Ser Tyr Gln Met Met Leu Pro Glu Ser Val Ala Ile Val Cys Ser

355 360 365

Pro Lys Phe Gln Glu Thr Gly Phe Phe Lys Leu Thr Asp His Gly Leu

370 375 380

Glu Glu Ile Ser Ser Cys Arg Gln Lys Gly Phe His Pro His Ser Lys

385 390 395 400

Asp Pro Pro Leu Phe Cys Ser Cys Ser His Val Thr Val Val Asp Arg

405 410 415

Ala Val Thr Ile Thr Asp Leu Arg

420

<210> 2

<211> 1910

<212> DNA

<213> Homo sapiens

<221> CDS

<222> 11..1282

<400> 2

cttggtcctg atgtctgacc atggagatgt gagcctcccg cccgaagacc gggtgagggc 60

tctctcccag ctgggtagtg cggtagaggt gaatgaagac attccacccc gtcggtactt 120

ccgctctgga gttgagatta tccgaatggc atccatttac tctgaggaag gcaacattga 180

acatgccttc atcctctata acaagtatat cacgctcttt attgagaaac taccaaaaca 240

tcgagattac aaatctgctg tcattcctga aaagaaagac acagtaaaga aattaaagga 300

gattgcattt cccaaagcag aagagctgaa ggcagagctg ttaaaacgat ataccaaaga 360

atatacagaa tataatgaag aaaagaagaa ggaagcagag gaattggccc ggaacatggc 420

catccagcaa gagctggaaa aggaaaaaca gagggtagca caacagaagc agcagcaatt 480

ggaacaggaa cagttccatg ccttcgagga gatgatccgg aaccaggagc tagaaaaaga 540
gcgactgaaa attgtacagg agtttgggaa ggtagaccct ggcctaggtg gcccgctagt 600
gcctgacttg gagaagccct ccttagatgt gttccccacc ttaacagtct catccataca 660
gccttcagac tgtcacacaa ctgtaaggcc agctaagcca cctgtggtgg acaggtcctt 720
gaaacctgga gcactgagca actcagaaag tattcccaca atcgatggat tgcgccatgt 780
ggtggtgcct gggcggctgt gcccacagtt tctccagtta gccagtgcca acactgcccg 840
gggagtggag acatgtggaa ttctctgtgg aaaactgatg aggaatgaat ttaccattac 900
ccatgttctc atccccaagc aaagtgctgg gtctgattac tgcaacacag agaacgaaga 960
agaacttttc ctcatacagg atcagcaggg cctcatcaca ctgggctgga ttcatactca 1020
ccccacacag accgcgtttc tctccagtgt cgacctacac actcactgct cttaccagat 1080
gatgttgcca gagtcagtag ccattgtttg ctcccccaag ttccaggaaa ctggattctt 1140
taaactaact gaccatggac tagaggagat ttcttcctgt cgccagaaag gatttcatcc 1200
acacagcaag gatccacctc tgttctgtag ctgcagccac gtgactgttg tggacagagc 1260
agtgaccatc acagaccttc gatgagcgtt tgagtccaac accttccaag aacaacaaaa 1320
ccatatcagt gtactgtagc cccttaattt aagctttcta gaaagctttg gaagtttttg 1380
tagatagtag aaaggggggc atcacctgag aaagagctga ttttgtattt caggtttgaa 1440
aagaaataac tgaacatatt ttttaggcaa gtcagaaaga gaacatggtc acccaaaagc 1500
aactgtaact cagaaattaa gttactcaga aattaagtag ctcagaaatt aagaaagaat 1560
ggtataatga acccccatat acccttcctt ctggattcac caattgttaa catttttttc 1620
ctctcagcta tccttctaat ttctctctaa tttcaatttg tttatattta cctctgggct 1680
caataagggc atctgtgcag aaatttggaa gccatttaga aaatcttttg gattttcctg 1740
tggtttatgg caatatgaat ggagcttatt actggggtga gggacagctt actccatttg 1800
accagattgt ttggctaaca catcccgaag aatgattttg tcaggaatta ttgttattta 1860
ataaatattt caggatattt ttcctctaca ataaagtaac aattaactta 1910

<210> 3

<211> 424

<212> PRT

<213> mouse

<400> 3

Met Ser Asp His Gly Asp Val Ser Leu Pro Pro Gln Asp Arg Val Arg
1 5 10 15
Ile Leu Ser Gln Leu Gly Ser Ala Val Glu Leu Asn Glu Asp Ile Pro
20 25 30
Pro Arg Arg Tyr Tyr Arg Ser Gly Val Glu Ile Ile Arg Met Ala Ser
35 40 45
Val Tyr Ser Glu Glu Gly Asn Ile Glu His Ala Phe Ile Leu Tyr Asn
50 55 60
Lys Tyr Ile Thr Leu Phe Ile Glu Lys Leu Pro Lys His Arg Asp Tyr
65 70 75 80
Lys Ser Ala Ile Ile Pro Glu Lys Lys Asp Ala Val Lys Lys Leu Lys
85 90 95
Ser Val Ala Phe Pro Lys Ala Glu Glu Leu Lys Thr Glu Leu Leu Arg
100 105 110
Arg Tyr Thr Lys Glu Tyr Glu Gln Tyr Lys Glu Arg Lys Lys Lys Glu
115 120 125
Glu Glu Glu Leu Ala Arg Asn Ile Ala Ile Gln Gln Glu Leu Glu Lys
130 135 140
Glu Lys Gln Arg Val Ala Gln Gln Lys Gln Lys Gln Leu Glu Gln Glu
145 150 155 160
Gln Phe His Ala Phe Glu Glu Met Ile Gln Arg Gln Glu Leu Glu Lys
165 170 175
Glu Arg Leu Lys Ile Val Gln Glu Phe Gly Lys Val Asp Pro Gly Pro
180 185 190
Cys Gly Pro Leu Leu Pro Asp Leu Glu Lys Pro Cys Val Asp Val Ala
195 200 205
Pro Ser Ser Pro Phe Ser Pro Thr Gln Thr Pro Asp Cys Asn Thr Gly

210 215 220

Met Arg Pro Ala Lys Pro Pro Val Val Asp Arg Ser Leu Lys Pro Gly

225 230 235 240

Ala Leu Ser Val Ile Glu Asn Val Pro Thr Ile Glu Gly Leu Arg His

245 250 255

Ile Val Val Pro Arg Asn Leu Cys Ser Glu Phe Leu Gln Leu Ala Ser

260 265 270

Ala Asn Thr Ala Lys Gly Ile Glu Thr Cys Gly Val Leu Cys Gly Lys

275 280 285

Leu Met Arg Asn Glu Phe Thr Ile Thr His Val Leu Ile Pro Arg Gln

290 295 300

Asn Gly Gly Pro Asp Tyr Cys His Thr Glu Asn Glu Glu Glu Ile Phe

305 310 315 320

Phe Met Gln Asp Asp Leu Gly Leu Leu Thr Leu Gly Trp Ile His Thr

325 330 335

His Pro Thr Gln Thr Ala Phe Leu Ser Ser Val Asp Leu His Thr His

340 345 350

Cys Ser Tyr Gln Met Met Leu Pro Glu Ser Ile Ala Ile Val Cys Ser

355 360 365

Pro Lys Phe Gln Glu Thr Gly Phe Phe Lys Leu Thr Asp Tyr Gly Leu

370 375 380

Gln Glu Ile Ser Thr Cys Arg Gln Lys Gly Phe His Pro His Gly Arg

385 390 395 400

Asp Pro Pro Leu Phe Cys Asp Cys Ser His Val Thr Val Lys Asp Arg

405 410 415

Ile Val Thr Ile Thr Asp Leu Arg

420

<210> 4

<211> 1384

<212> DNA

<213> homosapiens

<221> CDS

<222> 56..1327

<400> 4

gtgacgtttc cggaagctct gactgtcatc cttcacgaaa gaacttattt gtccaatgtc 60

tgaccatggg gatgtgagcc tcccacccca agaccgggtg aggattctgt cccaacttgg 120

gagtgcagtt gagttaaatg aagacattcc accccgtcgc tactaccgct ccggtgttga 180

gatcatccgc atggcgtccg tttactcgga agaaggcaac attgaacatg cctttatcct 240

ctacaacaag tacatcacgc tgtttattga aaaacttccg aaacaccgag actacaaatc 300

agctatcatt cctgagaaga aagatgctgt caagaaatta aagagcgtcg ctttccctaa 360

agcggaagag ctgaagacag agctcttgag aagatacacc aaagaatatg agcagtataa 420

agagcgaaag aaaaaggaag aagaggaact tgcccgaaat atcgccatcc agcaagagtt 480

ggaaaaagaa aaacagaggg ttgctcagca gaagcagaag cagctagagc aggagcaatt 540

ccatgccttt gaggagatga tccagaggca ggagctggaa aaagaacggc tgaaaattgt 600

tcaagagttc gggaaggtag accctggccc ctgcgggcct ctgctccctg atctggaaaa 660

gccttgtgta gatgtggccc ccagctcacc gttctcgccc acgcagactc cagactgtaa 720

cacaggcatg aggccagcta agccacctgt ggtggacagg tccctgaaac ctggagcgtt 780

aagcgtcata gaaaatgttc ccaccattga aggcctgcgc cacatcgtgg tgccccgtaa 840

tctgtgctca gaatttctcc agcttgccag tgccaatacc gccaaaggca ttgaaaccta 900

tggagtcctc tgtggaaaac tgatgagaaa tgaattcaca atcacacatg ttctcatccc 960

cagacaaaat ggtgggcctg attattgcca cacggagaat gaagaagaaa ttttctttat 1020

gcaggatgac cttggactcc tcactcttgg ctggatccat actcatccaa cccaaacggc 1080

ctttctgtcc agtgtggatc tccacactca ctgctcctac caaatgatgt taccagagtc 1140

catcgcaatc gtctgttccc caaagttcca ggaaactgga ttctttaagc taactgacta 1200

tggtcttcaa gagatttcaa cctgccggca gaaaggcttt cacccccatg gcagagaccc 1260

accgctgttc tgtgactgca gccatgtcac tgtcaaggac agaattgtga cgatcacaga 1320

ccttcgataa atctcaaatc atgaaccagg gagatggatc actgggtaac agcacttgtc 1380

acca 1384

Full Name of Sixth Inventor	FAMILY NAME	FIRST GIVEN NAME	SECOND GIVEN NAME	
Residence & Citizenship	CITY	STATE OR COUNTRY	COUNTRY OF CITIZENSHIP	
Post Office Address	ADDRESS	CITY	STATE OR COUNTRY	ZIP CODE

I further declare that all statements made herein of my own knowledge are true, and that all statements on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

1st Inventor _____ Date June 22, 2001
Kazuo SUGAMURA

2nd Inventor _____ Date June 22, 2001
Nobuyuki TANAKA

3rd Inventor _____ Date _____

4th Inventor _____ Date _____

5th Inventor _____ Date _____

6th Inventor _____ Date _____

The above application may be more particularly identified as follows:

U.S. Application Serial No. _____ Filing Date May 10, 2001

Applicant Reference Number 99-F-054PCT-US/YS Atty Docket No. 2001_0572A

Title of Invention PROTEIN AMSH AND cDNA THEREOF